Annex 1

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EUROPEAN PHARMACOPOEIA

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CAPSULES

Capsulae

The requirements of this monograph do not necessarily apply to preparations that are presented as capsules intended for use other than by oral administration. Requirements for such preparations may be found, where appropriate, in other general monographs, for example Rectal preparations (1145) and Vaginal preparations (1164).

DEFINITION

Capsules are solid preparations with hard or soft shells of various shapes and capacities, usually containing a single dose of active substance. They are intended for oral administration.

The capsule shells are made of gelatin or other substances, the consistency of which may be adjusted by the addition of substances such as glycerol or sorbitol. Excipients such as surface-active agents, opaque fillers, antimicrobial preservatives, sweeteners, colouring matter authorised by the competent authority and flavouring substances may be added. The capsules may bear surface markings.

The contents of capsules may be solid, liquid or of a paste-like consistency. They consist of one or more active substances with or without excipients such as solvents, diluents, lubricants and disintegrating agents. The contents do not cause deterioration of the shell. The shell, however, is attacked by the digestive fluids and the contents are released.

Where applicable, containers for capsules comply with the requirements of *Materials used for the manufacture of containers* (*3.1* and subsections) and *Containers* (*3.2* and subsections).

Several categories of capsules may be distinguished:

- hard capsules,
- soft capsules,
- gastro-resistant capsules,
- modified-release capsules,
- cachets.

PRODUCTION

In the manufacture, packaging, storage and distribution of capsules, suitable means are taken to ensure their microbial quality; recommendations on this aspect are provided in the text on *Microbiological quality of pharmaceutical preparations* (*5.1.4*).

TESTS

Uniformity of content (*2.9.6*). Unless otherwise prescribed or justified and authorised, capsules with a content of active substance less than 2 mg or less than 2 per cent of the total mass comply with test B for uniformity of content of single-dose preparations. If the preparation has more than one active substance, the requirement applies only to those ingredients which correspond to the above conditions.

Uniformity of mass (*2.9.5*). Capsules comply with the test for uniformity of mass of single-dose preparations. If the test for uniformity of content is prescribed for all the active substances, the test for uniformity of mass is not required.

Dissolution. A suitable test may be carried out to demonstrate the appropriate release of the active substance(s), for example one of the tests described in *Dissolution test for solid dosage forms* (*2.9.3*).

Where a dissolution test is prescribed, a disintegration test may not be required.

STORAGE

Store at a temperature not exceeding 30 °C.

LABELLING

The label states the name of any added antimicrobial preservative.

Hard capsules

DEFINITION

Hard capsules have shells consisting of two prefabricated cylindrical sections one end of which is rounded and closed, the other being open.

PRODUCTION

The active substance(s) usually in solid form (powder or granules) are filled into one of the sections which is then closed by slipping the other section over it. The security of the closure may be strengthened by suitable means.

TESTS

Disintegration. Hard capsules comply with the test for disintegration of tablets and capsules (*2.9.1*). Use *water R* as the liquid medium. When justified and authorised, *0.1 M hydrochloric acid* or *artificial gastric juice R* may be used as the liquid medium. If the capsules float on the surface of the water, a disc may be added. Operate the apparatus for 30 min, unless otherwise justified and authorised and examine the state of the capsules. The capsules comply with the test if all 6 have disintegrated.

Soft capsules

DEFINITION

Soft capsules have thicker shells than those of hard capsules. The shells consist of one part and are of various shapes.

PRODUCTION

Soft capsules are usually formed, filled and sealed in one operation but for extemporaneous use, the shell may be prefabricated. The shell material may contain an active substance.

Liquids may be enclosed directly; solids are usually dissolved or dispersed in a suitable vehicle to give a solution or dispersion of a paste-like consistency.

There may be partial migration of the constituents from the capsule contents into the shell and vice versa because of the nature of the materials and the surfaces in contact.

TESTS

Disintegration. Soft capsules comply with the test for disintegration of tablets and capsules (*2.9.1*). Use *water R* as the liquid medium. When justified and authorised, *0.1 M hydrochloric acid* or *artificial gastric juice R* may be used as the liquid medium. Add a disc to each tube. Liquid active substances dispensed in soft capsules may attack the disc; in such circumstances and where authorised, the disc may be omitted. Operate the apparatus for 30 min, unless otherwise justified and authorised and examine the state of the capsules. If the capsules fail to comply because of adherence to the discs, repeat the test on a further 6 capsules omitting the discs. The capsules comply with the test if all 6 have disintegrated.

Modified-release capsules

DEFINITION

Modified-release capsules are hard or soft capsules in which the contents or the shell or both contain special excipients or are prepared by a special process designed to modify the rate, the place or the time at which the active substance(s) are released.

Modified release capsules include prolonged-release capsules and delayed-release capsules.

PRODUCTION

A suitable test is carried out to demonstrate the appropriate release of the active substance(s).

Gastro-resistant capsules

DEFINITION

Gastro-resistant capsules are delayed-release capsules that are intended to resist the gastric fluid and to release their active substance or substances in the intestinal fluid. Usually they are prepared by filling capsules with granules or with particles covered with a gastro-resistant coating or in certain cases, by providing hard or soft capsules with a gastro-resistant shell (enteric capsules).

PRODUCTION

For capsules filled with granules or filled with particles covered with a gastro-resistant coating, a suitable test is carried out to demonstrate the appropriate release of the active substance(s).

TESTS

Disintegration. For capsules with a gastro-resistant shell carry out the test for disintegration (*2.9.1*) with the following modifications. Use *0.1 M hydrochloric acid* as the liquid medium and operate the apparatus for 2 h, or other such time as may be authorised, without the discs. Examine the state of the capsules. The time of resistance to the acid medium varies according to the formulation of the capsules to be examined. It is typically 2 h to 3 h but even with authorised deviations it must not be less than 1 h. No capsule shows signs of disintegration or rupture permitting the escape of the contents. Replace the acid by *phosphate buffer solution pH 6.8 R*. When justified and authorised, a buffer solution of pH 6.8 with added pancreas powder (for example, 0.35 g of *pancreas powder R* per 100 ml of buffer solution) may be used. Add a disc to each tube. Operate the apparatus for 60 min and examine the state of the capsules. If the capsules fail to comply because of adherence to the discs, repeat the test on a further 6 capsules omitting the discs. The capsules comply with the test if all 6 have disintegrated.

Dissolution. For capsules prepared from granules or particles already covered with a gastro-resistant coating, a suitable test is carried out to demonstrate the appropriate release of the active substance(s), for example the test described in *Dissolution test for solid dosage forms* (*2.9.3*).

Cachets

DEFINITION

Cachets are solid preparations consisting of a hard shell containing a single dose of one or more active substances. The cachet shell is made of unleavened bread usually from rice flour and consists of 2 prefabricated flat cylindrical sections. Before administration, the cachets are immersed in water for a few seconds, placed on the tongue and swallowed with a draught of water.

LABELLING

The label states the method of administration of the cachets.

01/2002:1239

CHEWING GUMS, MEDICATED

Masticabilia gummis medicata

DEFINITION

Medicated chewing gums are solid, single-dose preparations with a base consisting mainly of gum that are intended to be chewed but not swallowed.

They contain one or more active substances which are released by chewing. After dissolution or dispersion of the active substances in saliva, chewing gums are intended to be used for:

- local treatment of mouth diseases,
- systemic delivery after absorption through the buccal mucosa or from the gastrointestinal tract.

PRODUCTION

Medicated chewing gums are made with a tasteless masticatory gum base that consists of natural or synthetic elastomers. They may contain other excipients such as fillers, softeners, sweetening agents, flavouring substances, stabilisers and plasticisers and authorised colouring matter.

Medicated chewing gums are manufactured by compression or by softening or melting the gum bases and adding successively the other substances. In the latter case, chewing gums are then further processed to obtain the desired gum presentation. The medicated chewing gums may be coated, for example, if necessary to protect from humidity and light.

Unless otherwise justified and authorised, a suitable test is carried out to demonstrate the appropriate release of the active ingredient(s).

In the manufacture, packaging, storage and distribution of medicated chewing gums, suitable means must be taken to ensure their microbial quality; recommendations related to this aspect are provided in the general chapter on *Microbiological quality of pharmaceutical preparations* (*5.1.4*).

TESTS

Uniformity of content (*2.9.6*). Unless otherwise prescribed or justified and authorised, medicated chewing gums with a content of active ingredient less than 2 mg or less than 2 per cent of the total mass comply with test A for uniformity of content of single-dose preparations. If the preparation contains more than one active substance, the requirement applies only to those active substances which correspond to the above conditions.

Uniformity of mass (*2.9.5*). Uncoated medicated chewing gums and, unless otherwise justified and authorised, coated medicated chewing gums comply with the test for uniformity of mass of single-dose preparations. If the test for uniformity of content is prescribed for all the active substances, the test for uniformity of mass is not required.

STORAGE

Store uncoated medicated chewing gums protected from humidity and light.